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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,134	07/11/2003	Gerold Schuler	106985-2 KGB	4429

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	
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03/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,134	SCHULER ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11,29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/15/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 2/16/10 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/15/10 has been entered.

Claim 9 has been amended.

Claims 9, 11, 29-30 are pending and are under examination.

2. Upon reconsideration, the species of activation stimulus consisting of mature dendritic cells is rejoined.

3. The rejection of the claims under 35 U.S.C. 102 is withdrawn in view of Applicant's amendment to the claims to recite that the CD4+CD25- T cells are anergized with an anergic state inducing agent "consisting of" activated CD4+CD25+ T cells.

4. The following are new grounds of rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9, 11, and 29-30 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A method for producing Tr1 like regulatory T cells comprising activating CD4+CD25+ T cells with an activation stimulus consisting of "mature dendritic cells" (Claim 9 and dependent claims 11, and 29-30).

A review of the specification fails to reveal support for the new limitations.

At pages 9-10 and 13-14, the specification discloses activating CD4+CD25+ T cells with anti-CD3/CD28 or with mature allogeneic dendritic cells. However, the instant claims have a much broader scope than what is disclosed by the instant specification, and encompass any mature dendritic cell, including syngeneic dendritic cells. This is very different than the use of allogeneic dendritic cells, as disclosed by the specification. For example, while allogeneic dendritic cells can directly stimulate T cells, syngeneic dendritic cells do not activate T cells unless they have been loaded with an exogenous antigen that the T cells are specific for. The specification does not discuss the use of syngeneic dendritic cells, or what type of exogenously presented antigens would be suitable for activating CD4+CD25+ T cells. Thus, it is clear the instant specification does not contemplate the use of syngeneic dendritic cells for activation of CD4+CD25+ T cells, as is encompassed by the instant claims.

7. Claims 9, 11, and 29-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for producing human Tr1 regulatory T cells by contacting CD4+CD25- T cells with an anergic state inducing agent consisting of activated CD4+CD25+ T cells and (a) plate-bound anti-CD3 and soluble anti-CD28; or (b) allogeneic mature dendritic cells,

does not reasonably provide enablement for:

A method for producing human Tr1 regulatory T cells by contacting CD4+CD25- T cells with an anergic state inducing agent consisting of activated CD4+CD25+ T cells.

The specification disclosure is insufficient to enable one skilled in the art to

practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable the method as broadly claimed. The instant claims are drawn to a method of producing human Tr1 like regulatory T cells by anergizing CD4+CD25- T cells by contacting with an anergic state inducing agent *consisting of* activated CD4+CD25+ T cells. The term "anergy" refers to an unresponsive state that can be induced in T cells by a variety of mechanisms. However, the state of the art is such that induction of anergy requires some type of stimulation through the T cell receptor (see Lehler et al., 2001, in particular). Likewise, anergizing CD4+CD25- T cells to induce regulatory T cells requires stimulation of the T cell receptor (see Chen et al., 2003, page 1875). Thus, inducing anergy to produce regulatory T cells from CD4+CD25- T cells by contacting with CD4+CD25+ T cells alone, in the absence of TCR stimulation, is highly unpredictable.

Given the unpredictability of the art, the instant specification must provide a

sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that CD4+CD25- T cells can be converted into Tr1 regulatory T cells when contacted with activated CD4+CD25+ T cells and anti-CD3/anti-CD28 or mature allogeneic dendritic cells, which act to stimulate the TCR of the CD4+CD25- T cells. The instant specification does not provide any examples wherein CD4+CD25- T cells are anergized by contact with activated CD4+CD25+ T cells alone, in the absence of TCR stimulation, as recited in the instant claims. Thus, based on the unpredictability of the art and that lack of guidance provided by the instant specification, it would require undue experimentation to produce Tr1 regulatory T cells with an anergic state inducing agent "consisting of" activated CD4+CD25+ T cells, as claimed.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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